



Mini-review on Natural Disintegrants in Pharmaceutical Formulations

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Authors' contributions

This work was carried out in collaboration among all authors. Author SUK designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors AGKN and KDSS managed the analyses of the study. Author AGKN managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Disintegrants are agents which are integrated to tablets and some encapsulated formulations in order to promote the breakup of the tablet and capsule "slugs" into more small fragments in an aqueous environment which thereafter increment the available surface area and promoting a more rapid release of the drug substance. The development of new excipients for potential use as disintegrant agent in tablet formulations continues to be of interest. This is because different disintegrant agents can be useful in promoting penetration of moisture and dispersion of the tablet matrix and disintegration of tablet has received considerable attention at present as an essential step in obtaining fast drug release. Natural polymers such as starches, gums, mucilage, and dried fruits utilized as binder, diluent, and disintegrants to increase the solubility of poorly water-soluble drug, decrease the disintegration time, and provide nutritional supplement. Natural disintegrants are safe and economical than synthetic disintegrants such as Polyvinylpyrrolidone (PVP). Therefore, in the present review, an attempt has been made to reveal the importance of the natural disintegrants in the pharmaceutical formulations.

Keywords: Natural disintegrants; synthetic disintegrants; mucilages.

1. INTRODUCTION

Tablet disintegration is an essential step for fast drug release. The bioavailability of the drug highlights the importance of the rapid disintegration of a tablet as a criterion to ensure uninterrupted drug dissolution behaviour. Disintegrants are substances or mixture of substances which are added in drug formulations which enhances dispersion or breakup of tablets and capsules into smaller particles for fast dissolution. Disintegrants are consist of a group of materials that on contact with water swell, hydrate, change in volume or form or react chemically to produce a disruptive change in the tablet [1] The disintegrants have the major function to resist the efficiency of the tablet binder and the physical forces which act under compression to compose the tablet. With the increase of the powerful of the binder, the disintegrating agents must be more efficacious for the tablet to release its medication. Ideally, it should allow the tablet to disrupt, not only into the granules from which it was compressed, but additionally into powder particles from which the granulation was yare [2]. There are two classes of disintegrants: traditional disintegrants, such as starch, and super disintegrants, which include croscarmellose sodium, crospovidone, and sodium starch glycolate [3]. The term super-disintegrants refer to substances which achieve disintegration faster than the substances conventionally used [4].

2. FACTORS AFFECTING THE PERFORMANCE OF DISINTEGRANTS

- Particle size
- Methods of disintegrant incorporation especially for wet granulation
- Applied compression force
- Moisture content
- Percentage of disintegrants used
- Compatibility with other excipients
- Hardness of the tablets,
- Nature of Drug substances
- Presence of surfactants,
- Mixing and types of addition [1,5]

3. CHARACTERISTICS OF AN IDEAL DISINTEGRANT

As disintegrants are used as excipients in the tablet formulation, it must adopt certain

criteria other than its swelling properties. The requirement that is to be placed on the tablet disintegrants should be clearly defined. The ideal disintegrants should have:

- I. Poor water solubility with good hydration capacity
- II. Poor gel formation
- III. Good flow properties
- IV. Good compressibility
- V. Inert, non-toxic
- VI. Requirement of least quantity
- VII. Absence tendency to form complexes with the drugs.
- VIII. Must be compatible with the other excipients and have desirable tableting properties [4,6,7].

3.1 Types of Disintegrants

Broadly speaking there are two (02) types of disintegrants [8].

- I. Natural disintegrants
- II. Synthetic disintegrants

The various disintegrants includes synthetic derivatives such as sodium carboxy methyl cellulose, cross povidone, sodium starch glycollate, cross carmellose sodium, and natural derivatives such as alginates, cellulose, agar, locust bean, pectin, tragacanth, chitosan and gum karaya [8]. It is proved from the studies that natural polymers are safer and more efficacious than the synthetic polymers [2].

3.2 Natural Disintegrants

At present, there are number of plant-based pharmaceutical excipients and various researchers have explored the utility of some of these plant-based materials as pharmaceutical disintegrants [4]. These disintegrating agents are natural in origin and are preferred over synthetic substances since they are relatively cheaper, profusely available, non-irritating and nontoxic in nature. The natural materials such as gums and mucilage have been extensively used in the field of drug delivery for their easy possibility, eco friendliness, and cost multitude of chemical modifications, potentially degradable and compatible as they are of natural origin. There are several gums and mucilage which are available and consist of super- disintegrating activity [7].

3.3 Mucilages as Disintegrants

3.3.1 Ispaghula

Ispaghula comprise of dried seeds of the plant *Plantago ovata* and it consist of mucilage which is present in the epidermis of the seeds. *Plantago ovata* have various pharmaceutical formulation characteristics like binding, disintegrating and sustaining properties. The seeds of *Plantago ovata* were soaked in distilled water for 48 hrs and then boiled for few minutes for complete release of mucilage into water. Then this material was squeezed through muslin cloth for filtering and separating out the marc. Then, an equal volume of acetone was added to the filtrate so as to precipitate the mucilage and to separate it. The separated mucilage was dried in oven at temperature less than 60°C. The mucilage of *Plantago ovata* is a recent innovation for its superdisintegration property when compared with Crosspovidone. It shows faster disintegration time than the superdisintegrant, Crosspovidone [7]. The study done on evaluating the disintegrating properties of the Seed Powder, Husk Powder and mucilage powder of *Plantago ovata* had shown comparison in super disintegrants. The isolated mucilage powder had exhibited faster drug dissolution and improved bioavailability, thereby helping in effective therapy and improved patient compliance. Thus, the isolated mucilage powder can be effectively used as disintegrants in tablet formulations [8].

3.4 Fenugreek Seed Mucilage

Trigonella Foenum-graceum which is commonly known as Fenugreek, is an herbaceous plant of the leguminous family. It has been used in wide applications such food, food additives, traditional medicine. The leaves and the ripe and unripe seeds of Trigonella Foenum-graceum are used as vegetables. Fenugreek has been used to treat colic flatulence, dysentery, diarrhoea, dyspepsia with loss of appetite, chronic cough, dropsy, enlargement of liver and spleen, rickets, gout, and diabetes. It is also used as gastro protective, anti urolithiatic, diuretic, antidandruff agent, anti-inflammatory agent and as antioxidant. The seed is stated to be a tonic [9]. It is widely used in post-natal care and to increase lactation in nursing mothers. Fenugreek seeds contain a high percentage of mucilage (a natural gummy substance present in the coatings of many seeds). It does not dissolve in water but forms a viscous tacky mass when exposed to fluids. Like other mucilage-containing substances, fenugreek

seeds swell up and become slick when they are exposed to fluids. The resulting soft mass is not absorbed by the body, but it passes through the intestines and triggers intestinal muscle contractions instead [10]. The seeds were powdered using pestle and mortar and 100 g of the powder was extracted with hexane to remove lipophilic compounds using a Soxhlet apparatus. To remove pigments and to deactivate enzyme, the defatted powder was boiled in ethanol for 20 min. This treated powder was then soaked in 10 litres water and the pH was adjusted to 3.5 using 0.5 M Hydrochloric acid. The mixture was stirred by a mechanical stirrer for 12 h and then filtered through filtration paper. The filtrate was centrifuged (5000 g) and the supernatant was concentrated in vacuum to 50% of its initial volume. The resulting solution was mixed with the same volume of 96% ethanol and stored in a refrigerator for 4 h. The precipitated mucilage was separated by centrifugation (5000 g). The collected mucilage was re-suspended in distilled water, agitated for 20 min and re-precipitated one more time to eliminate chloride ions and other impurities. Finally, the residue was washed with diethyl ether and acetone and dried overnight at 45°C, resulting in an off-white powder [11].

3.5 Guar Gum

Guar gum is a galactomannan which is commonly used in cosmetics, food products and in pharmaceutical formulations. Guar gum is mainly consisting of high molecular weight (approximately 50,000-8,000,000) polysaccharides composed of galactomannans and is obtained from the endosperm of the seed of the guar plant, *Cyamopsis tetragonaloba* (L) Taub. (Synonym *Cyamopsis psoraloides*). It is used as a thickener, stabilizer, and emulsifier, and approved in most areas of the world (e.g. EU, USA, Japan, and Australia) [12]. Its synonyms are Galactosol; guar flour; jaguar gum; meprogat; meyprodor. Guar gum is investigated in the production of sustained release matrix tablets in the place of cellulose derivatives such as methylcellulose. In pharmaceutical industry, guar gum is used in solid-dosage forms as a binder and as a disintegrant, and used in oral and topical products as a suspending, thickening, and stabilizing agent. It is also used as a controlled-release carrier. Guar gum has also been examined for use in colonic drug delivery. [13,14] according to Jani GK et al., study conducted for isolation of mucilage, first the fresh plant materials were collected and washed with water to remove dirt and debris, and it was

allowed to dry. Then, the powdered material was soaked in water for 5–6 hours, then was boiled for 30 min, and allowed standing for 1 h so that all the mucilage was released into the water. The material was then squeezed from an eight muslin bag to remove the marc from the solution. Following this, three volumes of acetone was added to the filtrate to precipitate the mucilage. The mucilage was separated, dried in an oven at a temperature less than 50°C, and the dried powder was passed through a No. 80 sieve and stored in a desiccator until required [14].

3.6 Gum Karaya

Gum karaya is a vegetable gum produced as an exudate by trees of the genus *Sterculia*. Gum karaya is chemically an acid polysaccharide composed of the sugars galactose, rhamnose, and galacturonic acid. Its uses limits as binder and disintegrant in the development of conventional dosage form since it has a high viscosity nature. Gum karaya has been investigated for its potential as a tablet disintegrant. Different results showed that modified gum karaya produces rapid disintegration of tablets. Gum karaya can be utilized as an alternative superdisintegrant to commonly available synthetic and semisynthetic superdisintegrants due to its low cost, biocompatibility as well as facile availability [2]. Gum Karaya is a negative colloid as well as a complex polysaccharide with high molecular weight. It yields galactose, rhamnose and galacturonic acid on hydrolysis. Gum Karaya occurs as a partially acetylated derivative. It is a dried exudation of *sterculia Urenstree* (Family Sterculiaceae). Its synonyms are Karaya, *sterculia*, Indian tragacanth, *Bassora tragacanth*, *kadaya*, *Kadira*, *katila*. Gum Karaya is compatible with other plant hydrocolloids as well as proteins and carbohydrates [10].

3.7 Mucilage of Linseed

The mucilage isolated from *Linum usitatissimum* L., commonly called as Linseed has showed very good disintegrating activity. This also has confirmed good swelling properties during isolation. A series of concentration of mucilage have been tested and it has been observed that concentration of 8% mucilage has showed least disintegrating time when compared with the starch which has been used as the reference standard. This type of natural disintegrates are beneficial when compared with costly synthetic

disintegrates. Studies have been revealed that low concentrations of Linseed powder as a disintegrate compared to starch [15].

4. DISCUSSION

Several studies confirm that utilization of natural mucilage is valuable with proven biocompatibility, safe, chemically inert and non-toxic. The higher availability of mucilage impact on the development of pharmaceutical products with less cost effective. It is also environmental friendly processing and biodegradable.

5. CONCLUSION

Natural gums and mucilage are cost-effective, eco-friendly, easy accessible, compared with synthetic disintegrates which prefers widely over synthetic disintegrates. These are widely employed in Pharmaceutical as well as food industry since they are safe and non-toxic to animals and human beings and are extracted from natural products such as plant exudates and seeds of land and marine sources. Almost all the mucilage and gums are partially soluble in water which they swell and easily makes a gel. Natural disintegrates plays an important role in pharmaceutical formulations in many ways over synthetic disintegrates.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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